REMARKS

Applicants and their representative respectfully acknowledge the time and courtesy extended by the Examiner, Ms. Channavajjala, in conducting the Interview of December 18, 2002. Relevant aspects of the Interview are reflected in the above amendments and following remarks.

The Amendments

The specification is amended to correct some obvious typographical errors pointed out during the Interview.

The composition and kit claims have been canceled to focus the prosecution here on the methods of treating a disease, disorder or symptom associated with deficient endogenous levels of estrogen in women. The recitation that the drospirenone is micronized is also incorporated into the independent claim as the prosecution has previously focused on this embodiment. Further, the independent claim is amended to recite that the patient is "a woman having a deficient endogenous level of estrogen" to make even more clear the distinction from the copending '227 application, as discussed below regarding the obviousness-type double patenting rejection. The other claim amendments are formal in nature and do not narrow the claims' scope. Applicants intend to pursue and preserve the right to pursue any canceled subject matter by continuing application(s).

The Claim Objections

The objections of claims 84 and 97 are rendered moot by the above amendments.

The Provisional Obviousness-type Double Patenting Rejection

The provisional rejection of claims 77, 81-83 and 85-136 under the doctrine of obviousness-type double patenting over claims 1, 3-7, 9-14, 16-19, 21, 22 and 36-40 of copending application Ser. No. 09/654,227, alone or in view of U.S. Patent No. 5,922,349 to Elliesen is respectfully traversed.

The claims of the copending application are all directed to compositions or kits, i.e., claims generally categorized as composition of matter claims. The claims of the copending application include no method claims, particularly not claims encompassing a method of treating a disease, disorder or symptom associated with deficient endogenous levels of estrogen in women. The instant claims are all directed to methods of treating a disease, disorder or symptom associated with deficient endogenous levels of estrogen in women, i.e., claims generally categorized as process claims.

As to the provisional rejection being based on the '227 claims alone, it is believed to be clear that this ground cannot be maintained. The composition of matter claims of '227 provide no suggestion at all of the instant method claims. The methods disclosed but not claimed in the '227 specification cannot be relied upon to support the obviousness-type double patenting rejection, even if they were relevant. The '227 disclosure is not prior art. As stated in General Foods Corp. v. Studiengesellschaft Kohle mbH, 23 USPQ2d 1839, 1840 (Fed. Cir. 1992), "the law of double patenting is concerned only with what patents claim. 'Double patenting,' therefore, involves an inquiry into what, if anything, has been claimed twice."

As to the provisional rejection based on the '227 claims in view of Elliesen '349, the

apparent position taken in the Office Action is that Elliesen '349 suggests that the compositions/kits claimed in '227 would be useful in a method of treating a disease, disorder or symptom associated with deficient endogenous levels of estrogen in women. Before dealing with the issue on the merits, the order of issuance of the relevant claim sets should be known to determine the appropriate action. When one of the claims sets is in position for patenting except for this issue, applicants will address the merits, as appropriate. It is noted that this is only a provisional application.

The Provisional Rejection and Rejection under 35 U.S.C. §103 over Copending Application No. 09/654,227

The claims were subject to both a provisional and regular rejection under 35 U.S.C. §103 over Copending Application No. 09/654,227 alleged to be prior art on the basis of 35 U.S.C. §102(e). (As confirmed at the Interview, the Office Action had a typographical error indicating No. 09/654,772 but the '227 application was intended.) It is not clear why there was more than just a provisional rejection, since no patent or publication has yet issued, but these issues are believed rendered moot in light of the following discussion.

As noted in the Office Action, for applications filed on or after November 29, 1999 (which this application was), the rejection(s) can be overcome by establishing that the claimed invention and the subject matter in the copending application forming the basis of rejection were commonly owned or subject to assignment to a common assignee at the time the invention was made; see 35 U.S.C. §103(c). To establish such herein, applicants hereby state, through their undersigned representative, that instant application, Ser. No. 09/757,688 and copending

application, Ser. No. 09/654,227, were, at the time the invention of the '688 application was made, commonly owned by the instant assignee, Schering Aktiengesellschaft. This statement is made in accordance with M.P.E.P. §706.02(l)(2). These rejections should, therefore, be withdrawn.

The Rejection under 35 U.S.C. §103 over Elliesen (WO 97/11680) in view of Lignieres (Clinical Therapeutics)

Elliesen is directed to a method for hormone replacement therapy by administering a combination of an estrogen and a progestogen to a female patient in need thereof. The invention involves a means by which the dosage applied can be readily adjusted by the patient and self-administered. This is achieved by providing the drugs in an extrudable form which is applied to a delivery surface having measuring indicia. See, e.g., pages 6-8, page 19, last paragraph, and the Figures. Elliesen prefers topical administration with a transdermal or transmucosal uptake (see, e.g., page 17, second full paragraph) and the extruded form of the drugs lends itself to this method. But Elliesen also generally refers to oral administration using such extruded compositions; see, e.g., page 19, first full paragraph. As progestogens, Elliesen provides a list of a dozen examples at page 15, including drospirenone.

As discussed at the Interview on December 18, 2002, Elliesen does not disclose or suggest the use of drospirenone in micronized form in its methods. The list of progestogens at page 15 begins with the word "micronized" followed by the word "progesterone" and then the other progestogens separated by commas. Applicants respectfully submit that the broadest reasonable interpretation of these disclosures, to one of ordinary skill in the art, is that the term

"micronized" applies only to progesterone and not to the other progestogens. As attested to by Dr. Elliesen (an inventor of the Elliesen reference) in a Declaration under 37 C.F.R. §1.132 to be submitted shortly, the phrase "micronized progesterone" was a standard phrase used in the art because it was known that progesterone needed to be provided in micronized form in order to be clinically relevant. See also, page 4, lines 3-5, of the instant specification. In fact, it is confirmed by the Lignieres reference that natural progesterone should be used in micronized form for adequate bioavailability. Thus, one of ordinary skill in the art would have understood that the use of "micronized" in Elliesen had a special connection with progesterone and would not be read as applying to the other progestogens also. Dr. Elliesen confirms that this was the understanding in writing the disclosure which became the Elliesen reference.

The Elliesen disclosure read as a whole further confirms this interpretation. After the listing of the progestogens on page 15 of WO 97/11680, there is a listing of 4 preferred synthetic progestogens, including drospirenone but not including progesterone. The term "micronized" does not appear in this listing. If the "micronized" term applied to all the progestins in the initial list, it would be inconsistent to not include it in the preferred list. Similarly, claim 12 of WO 97/11680 recites 3 synthetic progestogens but does not recite that they are micronized. Further, it is noted that the progestogen used in the Examples 1-3 is not progesterone and is not micronized. Thus, the balance of the disclosure is consistent with applicants' position that the reasonable interpretation of Elliesen is that the "micronized" term applies only to progesterone and micronized drospirenone is not taught or suggested.

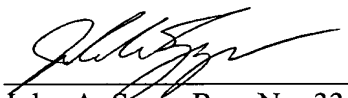
The Lignieres reference was relied upon in the Office Action as allegedly suggesting that it would have been obvious to one of ordinary skill in the art to use drospirenone in micronized

form for an HRT method, such as that of Elliesen. The teaching in Lignieres, however, relates only to progesterone (i.e., natural progesterone) and not broadly to progestogens, as argued in the Office Action. But, as discussed above, applying micronization to progesterone is a special case and, thus, the Lignieres teaching that progesterone has increased bioavailability when micronized would not have motivated one of ordinary skill in the art to micronize a different compound, e.g. drospirenone, for use in an HRT method involving oral administration. Thus, no *prima facie* case of obviousness is established on the record and the rejection under 35 U.S.C. §103 should be withdrawn. During the Interview, the Examiner raised the question of whether some unspecified comparative data could be provided which showed that the claimed method had unexpected advantages. Applicants respectfully urge that, because no *prima facie* case of obviousness is established on the record, a showing of unexpected advantages is not necessary.

It is submitted that the claims are in condition for allowance. But the Examiner is kindly invited to contact the undersigned to discuss any unresolved matters.

The Commissioner is hereby authorized to charge any fees associated with this response or credit any overpayment to Deposit Account No. 13-3402.

Respectfully submitted,



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VERSION WITH MARKINGS TO SHOW CHANGES MADE

The specification and claims have been amended as follows:

IN THE SPECIFICATION

Amend the paragraph at page 4, lines 21-23, to read as follows:

Apart ~~form~~ from the active substances themselves, it is envisaged that an ester or prodrug of drospirenone may be employed in the present composition, e.g., an oxyiminopregnane carbolactone as disclosed in WO 98/24801.

Amend the paragraph at page 9, lines 17-21, to read as follows:

In preferred embodiments, the dose of DRSP corresponds to 15 to 70 mg per cycle, such as 20 to 60 mg per cycle, particularly 40 to 60 mg per cycle. The length of the cycle, as stated *supra* may vary from ~~21to31~~ 21 to 31 days. Viewed otherwise, a composition may comprise of an amount of DRSP corresponding to a daily dose ranging from 0.25 to 10, such as about 0.25 to 8, 0.25 to 6, 0.25 to 5, 0.5 to 4.5, 1 to 4, and 1.5 to 3.5 mg.

IN THE CLAIMS

Cancel claims 77, 81-83, 85-89, 97, 120-121 and 123-133 and 135-136 without prejudice or disclaimer.

Amend claims 90, 92-95 and 99 to read as follows (a marked up version of the amended claims is in an appendix attached hereto):

90. (Twice Amended) A method of treating ~~and preventing diseases, disorders and symptoms~~ a disease, disorder or symptom associated with deficient endogenous levels of estrogen in women comprising orally administering, for at least one cycle of from 21 to 31 days, to a woman having a deficient endogenous level of estrogen;

an estrogen in a sufficient amount to alleviate said ~~diseases, disorders and symptoms,~~ disease, disorder or symptom,

and micronized drospirenone in a sufficient amount to protect the endometrium from adverse effects of estrogen~~,~~

~~said administering being by oral means~~.

92. (Amended) A method according to claim 90, wherein the ~~diseases, disorders and symptoms are~~ disease, disorder or symptom is selected from the group ~~comprising including~~ consisting of hot flushes, sweating attacks, palpitations, sleep disorders, mood changes, nervousness, anxiety, poor memory, loss of confidence, loss of libido, poor concentration, diminished energy, diminished drive, irritability, urogenital atrophy, atrophy of the breasts, cardiovascular disease, changes in hair distribution, thickness of hair, changes in skin condition and ~~or for the prevention or management of~~ osteoporosis.

93. (Amended) A method according to claim 92, wherein the ~~diseases, disorders and symptoms are~~ disease, disorder or symptom is selected from the group ~~comprising including~~ consisting of hot flushes, sweating attacks, palpitations, sleep disorders, mood changes, nervousness, anxiety, urogenital atrophy, atrophy of the breasts and ~~or for the prevention or management of~~ osteoporosis.

94. (Twice Amended) A method according to claim 90, wherein the estrogen is selected from the group consisting of ~~estrogen is selected from the group consisting of~~ estradiol, estradiol sulfamates, estradiol valerate, estradiol benzoate, ethinyl estradiol, estrone, estriol, estriol succinate, ~~and~~ conjugated estrogens~~, including conjugated equine estrogens such as estrone~~

~~sulfate, 17β-estradiol sulfate, 17α-estradiol sulfate, equilin sulfate, 17β-dihydroequilin sulfate, 17α-dihydroequilin sulfate, equilenin sulfate, 17β-dihydroequilenin sulfate and 17α-dihydroequilenin sulfate or~~ and mixtures thereof.

95. (Amended) A method according to claim 94, wherein the estrogen is selected from the group consisting of estradiol, estradiol sulfamates, estradiol valerate, estradiol benzoate, estrone, and estrone sulfate ~~or~~ and mixtures thereof.

99. (Amended) A method according to claim ~~90~~ 96, wherein the estradiol is in micronized form.